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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,949	07/27/2006	M Bishr Omary	STAN-297	1285

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,949	OMARY ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-14* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-7 (in part), drawn to a method for detecting a predisposition to liver disease by analyzing a genotype of keratin K8 by analyzing nucleic acids.

Group II, claims 1-7 (in part), drawn to a method for detecting a predisposition to liver disease by analyzing a genotype of keratin K18 by analyzing nucleic acids.

Group III, claims 1-5 and 8 (in part), drawn to a method for detecting a predisposition to liver disease by analyzing a genotype of keratin K8 by analyzing proteins.

Group IV, claims 1-5 and 8 (in part), drawn to a method for detecting a predisposition to liver disease by analyzing a genotype of keratin K18 by analyzing proteins.

Group V, claims 1-5 (in part), drawn to a method for detecting a predisposition to liver disease by analyzing a phenotype of keratin K8.

Group VI, claims 1-5 (in part), drawn to a method for detecting a predisposition to liver disease by analyzing a phenotype of keratin K18.

Group VII, claim 9 (in part), drawn to a method for screening for an agent that affects susceptibility to liver disease by contacting a polypeptide with an agent.

Group VIII, claim 9 (in part), drawn to a method for screening for an agent that affects susceptibility to liver disease by contacting a cell comprising a nucleic acid with an agent.

Group IX, claim 9 (in part), drawn to a method for screening for an agent that affects susceptibility to liver disease by contacting a non-human transgenic animal with an agent.

Group X, claims 10-12, drawn to a polypeptide.

Group XI, claim 13, drawn to an antibody.

Group XII, claim 14, drawn to a polynucleotide.

2. The inventions listed as Groups I-XII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A 371 case is considered to have unity of invention only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression "special technical feature" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. In the instant application, the claimed linking technical feature of mutations in the keratin K8 gene was known in the art at the time the invention was made. For example, Ku (The New England Journal of Medicine, 2001; cited in the IDS of 11/17/05), Ku (Gastroenterology. 2002. 122(4): 80; cited in the IDS of 11/17/05) and Ku (Molecular Biology of the Cell, 2001; cited in the IDS of 11/17/05) each teach methods for detecting the presence of mutations in the keratin 8 gene. In particular, Ku analyzed the keratin 8 gene of patients having liver disease and normal control individuals for the presence of mutations. Ku detected the presence of the Y53H and G61C mutations in the keratin 8 gene of patients having cryptogenic liver disease. These mutations were not found in patients with other types of liver disease or in control patients. Accordingly, Ku concluded that the Y53H and G61C mutations are associated with the occurrence of cryptogenic liver disease. While Ku does not

specifically exemplify methods for diagnosing liver disease by detecting the Y53H or G61C mutations, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the detection method of Ku to the diagnosis of cryptogenic liver disease since Ku teaches that the presence of the keratin 8 Y53H and G61C mutations are associated with the occurrence of cryptogenic liver disease. One would have been motivated to have done so in order to have generated a rapid, noninvasive and effective means for predicting a patient's susceptibility to cryptogenic liver disease. Thus, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention.

Further, Groups X-XII are additionally drawn to multiple, distinct products lacking the same or corresponding special technical features. The nucleic acids of groups XIII are composed of nucleotides and function in, e.g., methods of nucleic acid hybridization or amplification. The special technical feature of the nucleic acids are the identity of its monomers which are nucleotides which determine its structure, properties and functions. In contrast, the special technical feature of the antibodies of group XI are its amino acid monomers. The amino acids are arranged in a specific tertiary structure wherein four subunits (2 light chains and 2 heavy chains) are joined via disulfide bonds. While antibodies bind to specific target antigens and function in immunological reactions, polynucleotides do not have these functional activities. The special technical feature of the proteins of group X are also its amino acid monomers. However, the primary and secondary structure of the proteins of group X are distinct from that of the antibodies of group XI. As the products differ from each other in structure, function, and

effect, they do not belong to a recognized class of chemical compound, or have both a "common property or activity" and a common structure as would be required to show that the inventions are "of a similar nature". Additionally, each of the recited groups I-IX are directed to methods having different functions and effects, and requiring the use of different reagents and the performance of different process steps. As such, each of the methods has a different objective and outcome and does not share a corresponding technical feature.

3. **Further restriction requirement applicable to inventions I-VI and X-XII**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a specific combination of:

K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 1149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; and K18 G339X

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include

all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claims 3-14 encompasses the species recited above

The following claim(s) are generic:

Claims 1-2 are generic with respect to inventions I-VI

No claims are generic with respect to inventions X-XII

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acids and proteins differ from one another with respect to the nucleotide and amino acid sequences, respectively. Specifically, each nucleic acid and protein contains a polymorphism that occurs at a distinct nucleotide or amino acid position and consists of a distinct nucleotide or amino acid. Thus, the chemical structure of each polymorphism and molecule containing the polymorphism differ from one another. Thus, the claimed nucleic acids and proteins, and methods of using the same, do not have both a "common property or activity" and a common structure as would be required to show that the inventions are "of a similar nature."

Applicant is thereby required to elect either one or a particular combination of the recited polymorphisms. Note that the election of the polymorphism must be consistent with the elected invention. That is, if Applicant elects a method for detecting a

predisposition to liver disease by assaying for a keratin K8 nucleic acid, then the elected polymorphism should be a polymorphism in the K8 nucleic acid.

4. **Further restriction requirement applicable to inventions VII, VIII and IX**

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are one or a specific combination of:

K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 1149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; K18 G339X; a deletion of K8; a deletion of K18; a deletion of K8 and K18; a mutant of K8 that alters K8 filament organization; and a mutant of K18 that alters K18 filament organization.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Claim 9 encompasses the species recited above.

No claims are generic.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Each of the recited nucleic acids and proteins differ from one another with respect to the nucleotide and amino acid sequences, respectively. Specifically, each nucleic acid and protein contains a polymorphism that occurs at a distinct nucleotide or amino acid position and consists of a distinct nucleotide or amino acid. Thus, the chemical structure of each polymorphism and molecule containing the polymorphism differ from one another. Thus, the claimed nucleic acids and proteins, and methods of using the same, do not have both a "common property or activity" and a common structure as would be required to show that the inventions are "of a similar nature."

Applicant is thereby required to elect either one or a particular combination of the recited polymorphisms.

5. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not

distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

/Carla Myers/
Primary Examiner, Art Unit 1634